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Heredia-Rizo, Alberto Marcos; Petersen, Kristian Kjær; Madeleine, Pascal; Arendt-Nielsen, Lars

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**CLINICAL OUTCOMES AND CENTRAL PAIN MECHANISMS ARE IMPROVED
AFTER UPPER TRAPEZIUS ECCENTRIC TRAINING IN FEMALE COMPUTER
USERS WITH CHRONIC NECK/SHOULDER PAIN**

Alberto Marcos Heredia-Rizo Ph.D.^{1,2,3*}, Kristian Kjær Petersen Ph.D.², Pascal Madeleine
Ph.D.³, Lars Arendt-Nielsen DMSc^{2,4}

¹ Department of Physiotherapy, Faculty of Nursing, Physiotherapy and Podiatry, University
of Sevilla, Sevilla, Spain

² Center for Neuroplasticity and Pain (CNAP), SMI, Department of Health Science and
Technology, School of Medicine, Aalborg University, Aalborg, Denmark

³ Sport Sciences, Department of Health Science and Technology, School of Medicine,
Aalborg University, Aalborg, Denmark

⁴ Center for Sensory-Motor Interaction, School of Medicine, Aalborg University, Aalborg,
Denmark

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post-doc. The research conducted by KKP throughout this period was independent of the company.

***Corresponding Author:**

Assistant Professor Alberto M. Heredia-Rizo, PT, Ph.D.

Department of Physiotherapy

Faculty of Nursing, Physiotherapy and Podiatry, University of Sevilla,

c/ Avicena s/n, 41009 Sevilla, Spain

Phone: +34 954486507, Fax: +34 954486527, E-mail: amheredia@us.es

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ABSTRACT

Objectives: The effects of eccentric exercises on clinical outcomes and central pain mechanisms are unclear in neck/shoulder pain (NSP). The aims were to 1) evaluate the clinical impact of unilateral eccentric training in female computer users with chronic NSP, 2) compare pressure pain sensitivity, temporal summation of pain (TSP), and conditioned pain modulation (CPM) in female office workers with and without NSP, and 3) assess sensitization and central pain responses after training.

Methods: In part A, twenty females with NSP were compared with 20 controls. In part B, the NSP group underwent a 5-week upper trapezius eccentric training program. Participants reported their pain intensity, and completed the Neck Disability Index, and the Disabilities of the Arm, Shoulder and Hand questionnaire. Pressure pain thresholds (PPTs) were assessed over the neck and forearm. Cuff algometry identified pain detection (PDT) and tolerance thresholds (PTT). TSP was evaluated by visual analogue scale pain scores during 10 repetitive cuff stimulations. CPM was calculated as the difference in PDT with and without a conditioning painful stimulus. Outcomes were measured at baseline and post-intervention. Pain intensities were collected at 3-month and 6-month follow-up.

Results: Pain and disability decreased post-intervention ($p < 0.05$), and at follow-ups ($p = 0.002$). The NSP group demonstrated reduced PTT ($p \leq 0.02$), but no differences in TSP ($p = 0.947$) or CPM ($p = 0.059$) compared with controls. After training, females with NSP improved CPM, PPTs, and PTT at the non-treated side ($p < 0.05$).

Discussion: Eccentric training improved pain and disability, reduced sensitization and enhanced CPM efficiency in female computer users with NSP.

Keywords: Clinical pain, computer work, intervention, musculoskeletal disorders, strength training.

INTRODUCTION

The annual prevalence of neck/shoulder pain (NSP) ranges between 30-50% in the working age population¹. NSP represents one of the most common work-related musculoskeletal disorder (WMSD)², and the leading cause of disability worldwide³. Computer use may increase the risk of suffering WMSDs in the neck/shoulder⁴, with conflicting evidence and many controversies on this issue^{5,6}. Almost 50% of office workers complain of NSP on a weekly basis⁷, and women report higher prevalence⁶ and pain intensity⁵, compared with men. Multiple factors influence the natural time course of NSP in office workers^{8,9}. Among them, persistent and widespread musculoskeletal pain can play a role in the development of a chronic condition within this population⁵.

No differences in response to experimental muscle pain stimulation have been reported in computer users with NSP compared with painfree controls⁸. It has been suggested, however, that the excitability of the central pain system may be altered in subgroups of office workers defined by high clinical pain intensity and low mechanosensitivity thresholds over the neck/shoulder⁸. Temporal summation of pain (TSP) and conditioned pain modulation (CPM) have been used to assess central pain gain and impaired pain inhibition in musculoskeletal pain conditions¹⁰. Enhanced TSP and/or impaired CPM have been shown in chronic pain conditions, such as osteoarthritis^{11,12}, fibromyalgia¹³, whiplash-associated disorders¹⁴, shoulder pain¹⁵, and in computer users with high NSP intensity⁸. There is promising evidence suggesting that measures of central pain modulation may be prognostic factors to predict the outcome after e.g. surgery^{16,17}, or pharmaceutical interventions¹⁸.

Strength exercise programs are effective in the management of neck and upper extremity WMSDs among office workers^{19,20}, which may prevent widespread hyperalgesia and dysfunctional central pain modulation^{8,21}, as a result of exercise-induced hypoalgesia²². The activation of descending pain-inhibitory mechanisms contribute to enhance pain modulation

after exercise^{22, 23}. Physical activity involving repeated eccentric contractions can lead to initial damages in the active muscles²⁴, but also to further protection against subsequent damages^{25, 26}, supporting the role of eccentric bouts in treating NSP²⁶. Eccentric contractions occur when the external force applied to the muscle surpasses the force produced by the muscle itself, resulting in a lengthening contraction (i.e. elongation of muscle fibers)²⁷. To date, the efficacy of eccentric training on clinical outcomes, local and widespread sensitization, and features of central pain mechanisms has not been investigated in NSP. The aims of this study were to 1) evaluate the clinical impact of unilateral eccentric training in female computer users with chronic NSP, 2) compare pressure pain sensitivity, temporal summation of pain (TSP), and conditioned pain modulation (CPM) in female office workers with and without NSP, and 3) assess sensitization and central pain responses after training. It was hypothesized that: 1) eccentric training would improve clinical outcomes, 2) computer users with NSP would show higher local and widespread sensitization, increased TSP, and impaired CPM compared with controls, and 3) the eccentric protocol would benefit pressure pain sensitivity and central pain modulation responses underlining the plasticity of the nociceptive system.

METHODS

Study Design

The study protocol was divided in two parts: in part A, a cross-sectional study was carried out including female computer users with or without persistent non-traumatic NSP. In part B, participants with chronic NSP underwent a 5-week eccentric training intervention.

Participants

For part A, 40 female computer users, aged between 23-67 years (mean age \pm SEM, 44.3 \pm 1.4) volunteered to participate. During part B, nineteen of the twenty subjects with NSP (mean age \pm SEM, 46.8 \pm 1.4) completed the eccentric training regime. Participants were

recruited through advertising at Aalborg University. Using a body map chart, non-specific NSP was defined as pain in the neck/shoulder area without any known cause, and provoked by maintained postures, movements, and/or palpation¹. Participants were included in the NSP group when their pain lasted more than 12 weeks²⁸, and they reported their worst pain within the last 24 hours and their average pain during the week before data collection to be > 2 on a 11-point Numeric Pain Rating Scale (NPRS)⁵. Females reporting no pain or occasional pain ≤ 2 on the NPRS were assigned to the control group. All subjects had to work for a minimum of four hours per day using a computer, should speak and understand English, and could not have been involved in regular strength training of the neck/upper extremities within the previous year. The exclusion criteria were: pregnancy; previous whiplash²⁹; a history of neurological or mental illnesses; consumption of pain killers within the last 24 hours; drug addiction, defined as a continued and compulsive use of cannabis, opioids or other recreational drugs; fibromyalgia³⁰; previous cervical spine or upper limb surgery; carpal tunnel syndrome³¹; concomitant injury or pain from the lumbar spine; and heart diseases or hypertension. The study was conducted in accordance with the Helsinki Declaration, and approved by the North Denmark Region Committee on Health Research Ethics, project number N-20160023.

Protocol

Outcomes were collected by the same examiner. Demographic and clinical data were initially collected. For part A, the outcome measures were assessed during a baseline session lasting 90 minutes. Part B included an eccentric training program for participants with NSP during five consecutive weeks, in line with previous research³². For each participant, training started 3-7 days after completing the baseline testing and took place during working hours and within the University facilities. The final session (post-intervention) was carried out within 3-

7 days after the last training session³². Self-reported pain intensities were also collected at 3-month and 6-month follow-up.

Clinical outcomes

Participants were asked to rate their worst pain within the last 24 hours and their average NSP intensity during the previous week, using a 11-point NPRS³³. Based on the Nordic musculoskeletal questionnaire³⁴, questions on pain and discomfort during the past 12 months were posed for the neck and shoulder region. The Danish version of the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire³⁵, and the Neck Disability Index (NDI)³⁶ were used to identify self-reported function. The NDI is a valid and reliable tool (ICC from 0.50 to 0.98)³⁷, frequently used to assess functionality in workplace interventions³¹. The DASH questionnaire is the most recommended scale to assess individuals with shoulder disorders³⁸. A 15-point global rating of change scale (GRCS) (from -7, “a very great deal worse” to +7, “a very great deal better”) was used as a patient-rated change measure to assess the efficacy of intervention³⁹. With the GRCS, participants were asked to compare the overall functional condition of their neck/shoulder from baseline to post-intervention. A score ≥ 5 was considered as “important improvement”³⁹.

Manual and Cuff Pressure Algometry

A handheld electronic pressure algometer (Somedic AB, Hörby, Sweden), with a 1-cm² contact probe was used. Pressure pain thresholds (PPTs), as the minimum necessary pressure force to evoke pain⁴⁰, were assessed on both sides. The algometer was perpendicular to the skin while applying a constant rate of 30 kPa/s, and participants had to press the handheld button when the pressure exerted turned to pain. Pressure algometry is reliable in healthy individuals ICC 0.91 (95% CI 0.82 - 0.97)⁴¹, and in neck pain ICC 0.78 - 0.93 (95% CI 0.53 - 0.97)³⁰. PPTs were measured twice over: 1) the middle point of the upper trapezius muscle belly, and 2) the muscle bellies of the extensor carpi radialis brevis and the extensor carpi

ulnar⁸. A point 40 mm downward from the lateral epicondyle was marked with a wax pencil. Then, two points were symmetrically located 20 mm anterior (extensor carpi radialis brevis) and 20 mm posterior (extensor carpi ulnaris) to the first point⁸. A 30-second break was used between assessments to prevent bruising⁴², and an average of the two measures over each site was calculated for the statistical analysis.

For cuff pressure algometry, a computer-controlled cuff-algometer (Nocitech and Aalborg University, Aalborg, Denmark)⁴³ was used to evaluate distal sensitization at both lower legs by means of pain detection (PDT) and tolerance threshold (PTT). A single 13-cm-wide cuff (VBM, Sulz am Neckar, Germany) was wrapped around the calf area, at the level with the maximum circumference⁴⁴. The cuff pressure was increased by 1 kPa/s, with the maximal pressure set up at 100 kPa. Participants had to rate their pain intensity on a 10-cm electronic Visual Analogue Scale (VAS), and to press a button to release the cuff inflation when the pain was unbearable (PTT). PDT was considered as the pressure corresponding to the first VAS rating ≥ 1 cm⁴⁵. Computer-controlled cuff algometry constitutes an examiner-independent procedure for assessment of pain, and shows good to excellent reliability in healthy subjects and patients with chronic pain up to one month^{43,46}.

Temporal Summation of Pain

TSP was collected from the lower leg corresponding to the painful/most painful neck/shoulder, and the same side matched on dominance for controls. Ten consecutive cuff pressure stimuli (1-second duration, and 1-second break interval) were delivered by inflating the cuff chamber at the same intensity than the PTT⁴⁵. During intervals, a non-painful pressure of 1 kPa was applied. Participants had to continuously rate their pain on the electronic VAS without returning to zero during breaks. TSP was defined as the difference between the mean VAS score from the 8th to the 10th stimulus (VAS-II) and the mean VAS

value from the 1st to the 4th stimulus (VAS-I) (e.g., VAS-II minus VAS-I)⁴⁴. A higher value indicates enhanced TSP.

Conditioned Pain Modulation

Experimental tonic pain was evoked on the contralateral leg (calf area) with a continuous cuff-induced painful stimulus, set at 70% of the PTT on that side (conditioning stimulus)⁴⁷, corresponding to a moderate pain intensity (approximately 5-6 on the VAS)⁴⁸.

Simultaneously, PDT and PTT were evaluated (test stimulus) on the leg corresponding to the painful/most painful side (NSP group), or the dominant side (control group). The conditioning stimulus was terminated when the PDT and PTT assessments were completed. The CPM-effect was defined as: 1) the difference between PDT during vs. before conditioning⁴⁷, and 2) the percentage increase in PDT when comparing baseline with scores during conditioning pain⁴⁵. A lower CPM value indicates a less efficient central pain inhibition.

Eccentric Training

The intervention consisted of ten sessions of approximately 25-30 minutes of a unilateral eccentric exercise of the upper trapezius. Training took place twice a week over 5 consecutive weeks, as neural activation increases after 4 weeks of eccentric training⁴⁹. A custom-built dynamic shoulder dynamometer (Aalborg University, Aalborg, Denmark) was used⁵⁰. Participants were seated with back support and no feet support. When required, a corselet was used to prevent uneven loading of the spine. During baseline, the maximal voluntary contraction (MVC) of the painful/most-painful side was assessed. Participants relaxed their shoulders, the dynamometer's pad was lowered to the shoulder's level (3 cm medial to the acromion), and they were encouraged to perform an isometric shrug shoulder force for 3 seconds³². The MVC was recorded three times (2-min break between every test), and the average value was used for individually adjusting the load during training. All

sessions started with a 5-min warm-up. After a 2-min break, participants sat in the dynamometer, and the range of shoulder elevation (highest and lowest vertical position) was measured for the affected side. During training, participants were instructed to perform the eccentric exercise counteracting the delivered downward vertical force from the highest to the lowest shoulder position. Three bouts of 10 repetitions at 60% of MVC_{init} (sessions 1-3), 8 repetitions at 70% of MVC_{init} (sessions 4-6) and 6 repetitions at 80% of MVC_{init} (sessions 7-10) were carried out, with a 3-second rest between contractions and a 2-minute break between bouts³².

Statistical Analysis

The sample size was based on detecting: 1) clinically significant differences in the comparison between groups of 20% on manual pressure algometry (estimated inter-individual coefficient of variation for measure of 20%)⁵¹; and 2) a difference in VAS during TSP of 1.5 cm (estimated standard deviation of 1.5 cm) between stimuli 10 and stimuli 1⁴⁵. Considering an alpha value of 0.05, and a desired power of 80%, eighteen participants were required per group (Epidat 3.1, Xunta de Galicia, Spain).

Statistical processing was carried out using the PASW Advanced Statistics (SPSS Inc, Chicago, IL), version 24.0. Data are reported as mean, standard error of the mean (SEM), and confidence intervals (95% CI). The Shapiro-Wilk test was used to test the normal distribution of the variables. For part A, mixed-model ANOVAs were used to compare the differences between groups on PPT, TSP and CPM. For part B, a repeated measures ANOVA was applied to assess changes in pain intensities, neck/shoulder function, sensitization and central pain responses from baseline to post-intervention. Bonferroni adjustment for post hoc multiple comparisons of pain intensities was used. For part A, the Spearman's rank test or Pearson product-moment correlation coefficient analysis with Bonferroni's correction were used to test for associations at baseline between clinical data (years working with computers,

working hours per week, and duration of symptoms), and outcome measures (pain intensities, neck/shoulder function, PPT over the painful side, TSP, and CPM). Statistical significance was set at a p value <0.05 .

RESULTS

One participant with NSP completed the manual pressure algometry evaluations, but was afraid of using the cuff pressure algometer and dropped out after baseline. A total of 19 participants were included in the treatment protocol, without occurrence of adverse reactions or dropouts (see figure 1).

Fifteen females with NSP (75%) reported bilateral symptoms, with fourteen of them mostly complaining of their right side, and with a mean pain duration in this group of 120 months (39-207 months). The number of working-hours per week using a computer were not different between groups ($p=0.742$). Females with NSP reported higher pain intensity ($p<0.001$), poorer levels of neck, shoulder and upper extremity functionality ($p\leq 0.001$), and had worked with computers statistically longer than controls ($p=0.030$) (table 1).

Clinical outcomes

Pain intensities and neck/shoulder disability decreased significantly at post-intervention ($p<0.05$), except for the DASH work module ($p=0.107$) (table 2). The reduction in worst pain during the last 24 hours and pain average within the previous week remained significant at 3-month and 6-month follow-up ($p=0.002$) (table 2). Ten participants (52.63%) reported an “important improvement” in the GRCS (score ≥ 5) after training.

Comparision of females with and without neck/shoulder pain

There were no differences between groups either for PPTs over the neck and forearm (all $p>0.05$) (figure 2A), or for PDTs at the lower legs: painful/dominant side [-2.6 kPa (95% CI: -7.9; 2.7 kPa), $F=0.977$, $p=0.329$], and contralateral side [-3.5 kPa (95% CI: -8.5; 1.4 kPa), $F=2.031$, $p=0.163$]. On the contrary, females with NSP reported significantly lower PTTs on

both lower extremities compared with controls: painful/dominant side [-8.8 kPa (95% CI: -16.1; -1.4 kPa), $F=5.935$, $p=0.020$], and contralateral side [-10.3 kPa (95% CI: -18.7; -1.8 kPa), $F=6.084$, $p=0.018$] (figure 3A).

The VAS scores during the 10 repeated cuff stimulations showed a significant progressive increase in both groups, illustrating the TSP effect. The analysis of the differences from VAS-II to VAS-I showed no group-effect ($F=0.004$, $p=0.947$) (figure 4A).

Finally, participants with NSP had a 30% lower CPM response in their PDT compared with controls, although differences between groups in their CPM efficiency (PDT during vs. before conditioning) were not statistically significant [-5.67 kPa (95% CI: -11.59; 0.25 kPa), $F=3.758$, $p=0.059$] (figures 5A and 5B).

Effect of training on pain sensitivity and central pain mechanisms

Following eccentric training, PPTs increased significantly over the neck and forearm ($p<0.001$) (figure 2B). A significant improvement was also observed for the PTT (7.1 ± 2.2 kPa) on the contralateral lower leg ($p=0.004$) (figure 3B).

For TSP, no within-subjects differences were observed between baseline and post-intervention ($p=0.497$) (figure 4B). Finally, PDT during conditioning was significantly higher than PDT without conditioning (27.1 ± 2.3 kPa vs. 19.5 ± 1.49 kPa, $p<0.001$) (figure 5A), indicating a within-group CPM-effect ($p=0.014$) (figure 5B).

Correlation Analysis

In females with NSP, a significant negative correlation was found at baseline between CPM and upper limb disability (DASH). No other significant correlations were observed (table 3).

DISCUSSION

We showed for the first time that a 5-week unilateral eccentric training regime of the upper trapezius improved clinical outcomes (pain intensity and disability) immediately after training in female computer users with long-lasting NSP. Changes in pain intensities

remained significant in the short and medium-term. CPM was negatively associated with self-reported measures of pain and function in females with NSP. Higher distal sensitization, by means of increased PTTs, was observed in the NSP group compared with controls. The eccentric training protocol enhanced CPM, and reduced local and widespread pressure pain sensitivity.

Clinical outcomes

Eccentric training significantly decreased pain intensities post-intervention and at follow-ups. These changes were above the minimal clinically important change of the NPRS (2.5 points)⁵². Improvements in disability also surpassed the clinically relevant threshold of the NDI (3.5 points)⁵², but not of the DASH (12.4 points)⁵³. These findings were consistent with the fact that 10 participants reported an “important improvement” after training in the GRCS. The GRCS is widely used in the clinical setting, although it is questionable to which extent patients are able to accurately recall their previous health state³⁹.

There is evidence for the efficacy of strength training for relieving and preventing NSP among office workers^{54, 55}. Especially, worksite physical activity programs are highly effective on reducing neck/shoulder symptoms in computer users^{56, 57}. One hour of exercise per week and flexibility to fit the training sessions into the work routine are key aspects to achieve a positive impact⁵⁸. Both of them were taken into account, which may help to understand the current positive findings. However, there is no consensus as to which specific exercises are the most effective^{56, 59}. Eccentric training not resulting in adverse effects is feasible when exercise intensity is gradually increased⁶⁰. Eccentric exercises have the potential to evoke centrally mediated changes in pain sensitivity⁶¹. As compared to concentric or isometric training, eccentric contractions result in a swift adaptation that can produce greater improvement in strength⁶², stimulate muscle growth and increase neural drive⁶³. Indeed, consecutive sessions of eccentric exercises may develop protection against

subsequent muscle damage, and decrease pain sensitivity and soreness²⁶. Eccentric exercise is known to result in delayed-onset muscle soreness when unaccustomed⁶⁴. However, the repetition of eccentric exercise result in protective adaptation, referred to as the repeated bout effect, which can be explained by the interaction of neural, mechanical and cellular mechanisms⁶⁵. Neural adaptation causes a shift in the recruitment of motor units and/or increased motor unit synchronization. Changes in the muscle viscoelastic properties represent the mechanical adaptation, while cellular adaptation is supported by evidence for serial sarcomere addition, inflammatory responses, and changes in excitation-contraction coupling⁶⁵. The repeated bout effect has also been reported as lack of mechanical sensitization²⁶, or hypoalgesia^{26, 65}. In line with the present findings, eccentric training ranging from 4- to 12-week duration provides relief pain, and improves function and mobility in patients with subacromial impingement syndrome^{66, 67}. This is the first study to address eccentric training in computer users with moderate intensity and long-lasting NSP. The present results are very promising, but further research is needed including randomised control trial setup.

Comparison of females with and without neck/shoulder pain

Contrary to the present findings, higher localized mechanical sensitivity to pain has been reported among NSP patients compared with controls^{29, 68-73}. More specifically, three of these studies addressed women^{68, 69, 73}, but only one of them included office workers⁶⁸. Conflicting to this latter study⁶⁸, previous research did not show higher local sensitization in computer users with chronic musculoskeletal pain compared to painfree participants^{8, 31}, which is in line with the present results. There is also mixed evidence for widespread hyperalgesia within this population. Female office workers with moderate neck pain and disability displayed generalized hypersensitivity compared with controls³¹. On the contrary, Ge et al.⁸ reported no differences in PPTs at a remote site (tibialis anterior) between computer users with or without

musculoskeletal pain in the neck/shoulder. In the current study, higher distal sensitization, as assessed by PTT at the lower legs, was found in the NSP group compared with control participants. Differences in sensory related thresholds at non-injured sites may reflect altered central pain processing in women with chronic NSP⁷³. However, whether the differences in PTTs represent true distal hyperalgesia in females with NSP, show a discrepancy in their willingness to tolerate pain compared with controls, or simply reflect certain psychological traits of the NSP group⁷⁴, remains unclear.

The conflicting findings among studies persist when stimuli other than mechanical (e.g., thermal or vibratory) are used⁷⁵. There are some plausible explanations to account for these differences. First, in females with NSP, pain hypersensitivity seems to depend on the type of painful stimuli⁷⁶, levels of pain and disability³¹, as well as pain duration⁵. The current sample reported mild disability (NDI between 9-29)³¹, thus less developed level of sensitization was to be expected^{31,70}. Second, the term non-traumatic NSP is heterogeneous⁷⁵. WMSDs in the neck/shoulder are the result of a complex relationship between individual, physical and psychosocial risk factors¹, thus subgrouping patients within this disorder may help to understand those individuals in which central sensitization may play a role⁷². For instance, different sensitization mechanisms are observed in acute or chronic mechanical neck pain⁷², and patients with radiating neck pain respond differently to nociceptive signals than those with localized neck pain⁷⁷. Likewise, widespread pain in the working population seems to be associated with aspects such as physical loading at work, age and sex⁷⁸. However, in the current study, conducting such analysis will not be sound due to the relatively low sample size. Finally, chronic NSP is generally episodic over a lifetime, hence nociceptive inputs are not permanent, which may prevent abnormal central pain modulation⁷⁵. Contrary to other musculoskeletal conditions, such as fibromyalgia¹³, back pain⁷⁹, and whiplash-associated disorders⁷¹, non-specific NSP did not result in generalized sensory hypersensitivity⁷¹.

No differences in central pain gain (as the difference in pain ratings between the first few and the last few stimuli)⁴⁴ were observed between the study groups. Contrary to these findings, females with pelvic pain⁸⁰, temporomandibular disorders⁸¹, and whiplash-associated disorders⁸² show enhanced TSP to thermal or mechanical stimuli. Chua et al.⁸³ observed conflicting responses in TSP after electrical stimuli in neck pain patients. Pain distribution (local or radiated) may influence central pain responses in neck pain⁷⁷. In fact, enhanced TSP has been described in radiating, but not in local neck pain⁷⁷. Likewise, psychological factors may be a modulating mechanism of central pain modulation responses⁸⁴. TSP can be calculated in different ways, such as the difference between the first five and last five stimuli when using a pinprick system⁸⁵, or by rating the first, fifth and tenth stimuli when using heat stimuli⁸⁶. These methodological differences should be considered when comparing studies.

Regarding CPM efficiency, there were no significant differences between groups. A possible explanation for this phenomenon is that CPM has no additive effect. CPM may fail when a conditioning pain stimulus is administered in the presence of two already existing pain stimuli (clinical pain and test stimulus). Therefore, the ongoing clinical pain may act as a conditioning stimulus that has already activated the descending and inhibiting pathways⁸⁷. Current evidence about central sensitization in non-specific NSP is inconclusive⁷⁵. In a similar study protocol and in line with the present findings, no differences in CPM were found between computer users with or without a low level of musculoskeletal pain⁸. The same findings have been reported in chronic isolated neck⁸³, or shoulder pain⁸⁸. The current study found that CPM was negatively correlated with self-reported disability, suggesting that ongoing pain intensity and disability may influence central pain processing, as observed in computer users with chronic pain⁸, and in painful knee osteoarthritis¹¹.

Effect of training on pain sensitivity and central pain mechanisms

The eccentric training augmented PPTs on the treated and non-treated sides above the 20% clinically meaningful threshold⁵¹. Training effects in the unexercised contralateral limb following unilateral strength training (cross-transfer) have been previously documented⁸⁹. Indeed, a contralateral repeated bout effect occurs after eccentric contractions, although the underlying physiological mechanisms remains unclear⁹⁰. Exercise-induced hypoalgesia has been confirmed following eccentric exercises of the upper trapezius²⁶, and wrist extensor muscles²⁵, suggesting that pain sensitivity could be normalized following repeated eccentric exercise⁶¹. Even as little as 2 minutes of daily resistance training results in reductions of pain in adults complaining of neck/shoulder symptoms⁹¹.

Previous research shows that TSP is modulated in healthy participants after short duration isometric exercises^{92,93}, and in presence of delayed onset muscle soreness⁹⁴, but not after eccentric exercises of jaw muscles⁹⁵. A submaximal aerobic exercise reduces TSP in chronic whiplash-associated disorders⁹⁶. Most of studies in this area assessed changes in TSP after a single exercise session, which does not reflect clinical practice. This is also the first study to evaluate changes following a 5-week training regime. The differences among studies could be understood based on the different stimuli used to evoke TSP, since mechanical stimuli have a less pronounced effect on pain modulation measurements⁹⁶. Besides, the degree of pain sensitivity⁹⁷, and psychosocial variables⁹⁸, seem to influence patients' capacity to modulate pain through exercise-induced hypoalgesia.

The successful management of pain with eccentric training may help to explain the improvement in CPM among females with NSP, since pain modulation seems to influence the efficacy of endogenous pain inhibition⁸⁷. This is clinically relevant because eccentric exercises could eventually prevent pain chronification through exercise-induced hypoalgesia²² and, therefore, help to avoid dysfunctional central pain modulation in the portion of NSP with moderate to severe intensity. Local exercises show widespread pain-

inhibitory effects, suggesting central response⁹⁹. Exercising may activate descending pain inhibitory pathways^{99, 100}. Furthermore, improvements in pain intensity after training are correlated with changes in intramuscular pain modulatory substances in women with chronic NSP¹⁰¹. Based on the contradictory findings of central pain gain and pain inhibitory mechanisms, it cannot be concluded that female computer users with NSP exhibit improved central pain modulation in response to eccentric exercises, but the results are promising in this sense.

Limitations

This study is explorative in nature, includes a small sample size and lacks of assessor blinding, thus results should be interpreted carefully. Without a control group for part B, it is difficult to assure that results after training are not influenced by a learning effect. In the NSP group, the baseline scores for the NDI and the DASH questionnaire represented “mild disability” and “no problem to work”, respectively, thus these outcomes were not assessed during follow-up. Work-related exposures may influence the prognosis of NSP¹⁰², and were not controlled in this study. Furthermore, participants were not specifically addressed for their general physical activity level. This could be a confounding factor for its influence on pain inhibitory and facilitatory mechanisms¹⁰³. Psychosocial features could have influenced TSP responses⁸⁴, but were not evaluated. Finally, it may be of interest to investigate the impact of a bilateral training program, the efficacy of repeated eccentric exercises on strength gains, and if different results could be expected on TSP and CPM with stimuli other than mechanical.

Conclusion

A worksite unilateral eccentric training program of 5-week duration resulted in clinically relevant improvements of pain and disability in female computer users with chronic NSP. Changes in pain intensity remained significant at follow-up assessments. This study revealed that female computer users with moderate level of NSP showed higher widespread sensitization, but no differences in central pain gain and CPM compared with controls. The eccentric protocol reduced local and distal pressure pain sensitivity, and enhanced CPM in participants with NSP.

REFERENCES

1. Côté P, van der Velde G, Cassidy JD, *et al.* The burden and determinants of neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008; **33**:S60-74.
2. Schneider E, Irastorza X, Copes S, *et al.* OSH in figures: Work-related musculoskeletal disorders in the EU: Facts and figures. Luxembourg: European Agency for Safety and Health at Work, 2010.
3. Vos T, Allen C, Arora M, *et al.* Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; **388**:1545-602.
4. Andersen JH, Fallentin N, Thomsen JF, Mikkelsen S. Risk factors for neck and upper extremity disorders among computers users and the effect of interventions: an overview of systematic reviews. *PLoS One* 2011; **6**:e19691.
5. Madeleine P, Vangsgaard S, Hviid Andersen J, *et al.* Computer work and self-reported variables on anthropometrics, computer usage, work ability, productivity, pain, and physical activity. *BMC Musculoskelet Disord* 2013; **14**:226.
6. Paksaichol A, Janwantanakul P, Purepong N, *et al.* Office workers' risk factors for the development of non-specific neck pain: a systematic review of prospective cohort studies. *Occup Environ Med* 2012; **69**:610-8.
7. Janwantanakul P, Pensri P, Jiamjarasrangsri V, Sinsongsook T. Prevalence of self-reported musculoskeletal symptoms among office workers. *Occup Med (Lond)* 2008; **58**:436-8.
8. Ge HY, Vangsgaard S, Omland Ø, *et al.* Mechanistic experimental pain assessment in computer users with and without chronic musculoskeletal pain. *BMC Musculoskelet Disord* 2014; **15**:412.

9. Hallman DM, Birk Jørgensen M, Holtermann A. Objectively measured physical activity and 12-month trajectories of neck-shoulder pain in workers: A prospective study in DPHACTO. *Scand J Public Health* 2017; **45**:288-98.
10. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. *Nat Rev Rheumatol* 2010; **6**:599-606.
11. Arendt-Nielsen L, Nie H, Laursen MB, *et al.* Sensitization in patients with painful knee osteoarthritis. *Pain* 2010; **149**:573-81.
12. Graven-Nielsen T, Wodehouse T, Langford RM, *et al.* Normalization of widespread hyperesthesia and facilitated spatial summation of deep-tissue pain in knee osteoarthritis patients after knee replacement. *Arthritis Rheum* 2012; **64**:2907-16.
13. Julien N, Goffaux P, Arsenault P, Marchand S. Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition. *Pain* 2005; **114**:295-302.
14. Curatolo M, Arendt-Nielsen L, Petersen-Felix S. Evidence, mechanisms, and clinical implications of central hypersensitivity in chronic pain after whiplash injury. *Clin J Pain* 2004; **20**:469-76.
15. Noten S, Struyf F, Lluch E, *et al.* Central Pain Processing in Patients with Shoulder Pain: A Review of the Literature. *Pain Pract* 2017; **17**:267-80.
16. Petersen KK, Graven-Nielsen T, Simonsen O, *et al.* Preoperative pain mechanisms assessed by cuff algometry are associated with chronic postoperative pain relief after total knee replacement. *Pain* 2016; **157**:1400-6.
17. Petersen KK, Simonsen O, Laursen MB, Arendt-Nielsen L. The role of preoperative radiological severity, sensory testing, and temporal summation on chronic postoperative pain following total knee arthroplasty. *Clin J Pain* 2018; **34**:193-197.
18. Grosen K, Fischer IW, Olesen AE, Drewes AM. Can quantitative sensory testing predict responses to analgesic treatment? *Eur J Pain* 2013; **17**:1267-80.

19. Pedersen MT, Andersen LL, Jørgensen MB, *et al.* Effect of specific resistance training on musculoskeletal pain symptoms: dose-response relationship. *J Strength Cond Res* 2013; **27**:229-35.
20. Sihawong R, Janwantanakul P, Sitthipornvorakul E, Pensri P. Exercise therapy for office workers with nonspecific neck pain: a systematic review. *J Manipulative Physiol Ther* 2011; **34**:62-71.
21. Koltyn KF. Exercise-induced hypoalgesia and intensity of exercise. *Sports Med* 2002; **32**:477-87.
22. Koltyn KF, Brellenthin AG, Cook DB, *et al.* Mechanisms of exercise-induced hypoalgesia. *J Pain* 2014; **15**:1294-304.
23. Naugle KM, Fillingim RB, Riley JL. A meta-analytic review of the hypoalgesic effects of exercise. *J Pain* 2012; **13**:1139-50.
24. Clarkson PM, Hubal MJ. Exercise-induced muscle damage in humans. *Am J Phys Med Rehabil* 2002; **81**:S52-69.
25. Delfa de la Morena JM, Samani A, Fernández-Carnero J, *et al.* Pressure pain mapping of the wrist extensors after repeated eccentric exercise at high intensity. *J Strength Cond Res* 2013; **27**:3045-52.
26. Kawczyński A, Samani A, Fernández-de-Las-Peñas C, *et al.* Sensory mapping of the upper trapezius muscle in relation to consecutive sessions of eccentric exercise. *J Strength Cond Res* 2012; **26**:1577-83.
27. Lindstedt SL, LaStayo PC, Reich TE. When active muscles lengthen: properties and consequences of eccentric contractions. *News Physiol Sci* 2001; **16**:256-61.
28. International Association for the Study of Pain. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. *Pain* 1986; **Suppl 3**:S1-226.

29. La Touche R, Fernández-de-Las-Peñas C, Fernández-Carnero J, *et al.* Bilateral mechanical-pain sensitivity over the trigeminal region in patients with chronic mechanical neck pain. *J Pain* 2010; **11**:256-63.
30. Ylinen J, Nykänen M, Kautiainen H, Häkkinen A. Evaluation of repeatability of pressure algometry on the neck muscles for clinical use. *Man Ther* 2007; **12**:192-7.
31. Johnston V, Jimmieson NL, Jull G, Souvlis T. Quantitative sensory measures distinguish office workers with varying levels of neck pain and disability. *Pain* 2008; **137**:257-65.
32. Vangsgaard S, Taylor JL, Hansen EA, Madeleine P. Changes in H reflex and neuromechanical properties of the trapezius muscle after 5 weeks of eccentric training: a randomized controlled trial. *J Appl Physiol (1985)* 2014; **116**:1623-31.
33. Jensen MP, Turner JA, Romano JM, Fisher LD. Comparative reliability and validity of chronic pain intensity measures. *Pain* 1999; **83**:157-62.
34. Kuorinka I, Jonsson B, Kilbom A, Vinterberg H, *et al.* Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. *Appl Ergon* 1987; **18**:233-7.
35. Herup A, Merser S, Boeckstyns M. [Validation of questionnaire for conditions of the upper extremity]. *Ugeskr Laeger* 2010; **172**:3333-6.
36. Lauridsen HH, O'Neill L, Kongsted A, Hartvigsen J. The Danish Neck Disability Index: New Insights into Factor Structure, Generalizability, and Responsiveness. *Pain Pract* 2017; **17**:480-93.
37. MacDermid JC, Walton DM, Avery S, *et al.* Measurement properties of the neck disability index: a systematic review. *J Orthop Sports Phys Ther* 2009; **39**:400-17.
38. Bot SD, Terwee CB, van der Windt DA, *et al.* Clinimetric evaluation of shoulder disability questionnaires: a systematic review of the literature. *Ann Rheum Dis* 2004; **63**:335-41.
39. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J Man Manip Ther* 2009; **17**:163-70.

40. Vanderweeën L, Oostendorp RA, Vaes P, Duquet W. Pressure algometry in manual therapy. *Man Ther* 1996; **1**:258-65.
41. Chesterton LS, Sim J, Wright CC, Foster NE. Interrater reliability of algometry in measuring pressure pain thresholds in healthy humans, using multiple raters. *Clin J Pain* 2007; **23**:760-6.
42. Nie H, Graven-Nielsen T, Arendt-Nielsen L. Spatial and temporal summation of pain evoked by mechanical pressure stimulation. *Eur J Pain* 2009; **13**:592-9.
43. Graven-Nielsen T, Vaegter HB, Finocchietti S, *et al.* Assessment of musculoskeletal pain sensitivity and temporal summation by cuff pressure algometry: a reliability study. *Pain* 2015; **156**:2193-202.
44. Petersen KK, Arendt-Nielsen L, Finocchietti S, *et al.* Age Interactions on Pain Sensitization in Patients with Severe Knee Osteoarthritis and Controls. *Clin J Pain* 2017; **33**:1081-7
45. Rathleff MS, Petersen KK, Arendt-Nielsen L, *et al.* Impaired conditioned pain modulation in young female adults with long-standing patellofemoral pain: A single blinded cross-sectional study. *Pain Med* 2016; **17**:980-8.
46. Vaegter HB, Graven-Nielsen T. Pain modulatory phenotypes differentiate subgroups with different clinical and experimental pain sensitivity. *Pain* 2016; **157**: 1480-8.
47. Andersen HH, Imai Y, Petersen KK, *et al.* Conditioning pain stimulation does not affect itch induced by intra-epidermal histamine pricks but aggravates neurogenic inflammation in healthy volunteers. *Somatosens Mot Res* 2016; **33**:49-60.
48. Graven-Nielsen T, Izumi M, Petersen KK, Arendt-Nielsen L. User-independent assessment of conditioning pain modulation by cuff pressure algometry. *Eur J Pain* 2017; **21**:552-61.
49. Baroni BM, Rodrigues R, Franke RA, *et al.* Time course of neuromuscular adaptations to knee extensor eccentric training. *Int J Sports Med* 2013; **34**:904-11.

50. Madeleine P, Nie H, Arendt-Nielsen L. Dynamic shoulder dynamometry: a way to develop delay onset muscle soreness in shoulder muscles. *J Biomech* 2006; **39**:184-8.
51. Prushansky T, Dvir Z, Defrin-Assa R. Reproducibility indices applied to cervical pressure pain threshold measurements in healthy subjects. *Clin J Pain* 2004; **20**:341-7.
52. Pool JJ, Ostelo RW, Hoving JL, *et al.* Minimal clinically important change of the Neck Disability Index and the Numerical Rating Scale for patients with neck pain. *Spine (Phila Pa 1976)* 2007; **32**:3047-51.
53. van Kampen DA, Willems WJ, van Beers LW, *et al.* Determination and comparison of the smallest detectable change (SDC) and the minimal important change (MIC) of four-shoulder patient-reported outcome measures (PROMs). *J Orthop Surg Res* 2013; **8**:40.
54. Andersen LL, Jørgensen MB, Blangsted AK, *et al.* A randomized controlled intervention trial to relieve and prevent neck/shoulder pain. *Med Sci Sports Exerc* 2008; **40**:983-90.
55. Sjögren T, Nissinen KJ, Järvenpää SK, *et al.* Effects of a workplace physical exercise intervention on the intensity of headache and neck and shoulder symptoms and upper extremity muscular strength of office workers: a cluster randomized controlled cross-over trial. *Pain* 2005; **116**:119-28.
56. Blangsted AK, Søgaard K, Hansen EA, *et al.* One-year randomized controlled trial with different physical-activity programs to reduce musculoskeletal symptoms in the neck and shoulders among office workers. *Scand J Work Environ Health* 2008; **34**:55-65.
57. Gram B, Andersen C, Zebis MK, *et al.* Effect of training supervision on effectiveness of strength training for reducing neck/shoulder pain and headache in office workers: cluster randomized controlled trial. *Biomed Res Int* 2014; **2014**:693013.
58. Andersen CH, Andersen LL, Gram B, *et al.* Influence of frequency and duration of strength training for effective management of neck and shoulder pain: a randomised controlled trial. *Br J Sports Med* 2012; **46**:1004-10.

59. Hagberg M, Harms-Ringdahl K, Nisell R, Hjelm EW. Rehabilitation of neck-shoulder pain in women industrial workers: a randomized trial comparing isometric shoulder endurance training with isometric shoulder strength training. *Arch Phys Med Rehabil* 2000; **81**:1051-8.
60. Isner-Horobeti ME, Dufour SP, Vautravers P, *et al.* Eccentric exercise training: modalities, applications and perspectives. *Sports Med* 2013; **43**:483-512.
61. Hosseinzadeh M, Andersen OK, Arendt-Nielsen L, Madeleine P. Pain sensitivity is normalized after a repeated bout of eccentric exercise. *Eur J Appl Physiol* 2013; **113**:2595-602.
62. Roig M, O'Brien K, Kirk G, *et al.* The effects of eccentric versus concentric resistance training on muscle strength and mass in healthy adults: a systematic review with meta-analysis. *Br J Sports Med* 2009 ;**43**:556-68.
63. Hedayatpour N, Falla D. Physiological and neural adaptations to eccentric exercise: Mechanisms and considerations for training. *Biomed Res Int* 2015; **2015**:193741.
64. Fridén J. Delayed onset muscle soreness. *Scand J Med Sci Sports* 2002; **12**:327-8.
65. McHugh MP. Recent advances in the understanding of the repeated bout effect: the protective effect against muscle damage from a single bout of eccentric exercise. *Scand J Med Sci Sports* 2003; **13**:88-97.
66. Vallés-Carrascosa E, Gallego-Izquierdo T, Jiménez-Rejano JJ, *et al.* Pain, motion and function comparison of two exercise protocols for the rotator cuff and scapular stabilizers in patients with subacromial syndrome. *J Hand Ther* 2018; **31**:227-237.
67. Bernhardsson S, Klintberg IH, Wendt GK. Evaluation of an exercise concept focusing on eccentric strength training of the rotator cuff for patients with subacromial impingement syndrome. *Clin Rehabil* 2011; **25**:69-78.
68. Levoska S. Manual palpation and pain threshold in female office employees with and without neck-shoulder symptoms. *Clin J Pain* 1993; **9**:236-41.

69. Coppeters I, De Pauw R, Kregel J, *et al.* Differences between women with traumatic and idiopathic chronic neck pain and women without neck pain: interrelationships among disability, cognitive deficits, and central sensitization. *Phys Ther* 2017; **97**:338-53.
70. Chien A, Sterling M. Sensory hypoaesthesia is a feature of chronic whiplash but not chronic idiopathic neck pain. *Man Ther* 2010; **15**:48-53.
71. Scott D, Jull G, Sterling M. Widespread sensory hypersensitivity is a feature of chronic whiplash-associated disorder but not chronic idiopathic neck pain. *Clin J Pain* 2005; **21**:175-81.
72. Javanshir K, Ortega-Santiago R, Mohseni-Bandpei MA, *et al.* Exploration of somatosensory impairments in subjects with mechanical idiopathic neck pain: a preliminary study. *J Manipulative Physiol Ther* 2010; **33**:493-9.
73. Sjörs A, Larsson B, Persson AL, Gerdle B. An increased response to experimental muscle pain is related to psychological status in women with chronic non-traumatic neck-shoulder pain. *BMC Musculoskelet Disord* 2011; **12**:230.
74. Kato F, Abe T, Kanbara K, *et al.* Pain threshold reflects psychological traits in patients with chronic pain: a cross-sectional study. *Biopsychosoc Med* 2017; **11**:13.
75. Malfliet A, Kregel J, Cagnie B, *et al.* Lack of evidence for central sensitization in idiopathic, non-traumatic neck pain: a systematic review. *Pain Physician* 2015; **18**:223-36.
76. Uthakhpur S, Prasert R, Paungmali A, Boontha K. Altered pain sensitivity in elderly women with chronic neck pain. *PLoS One* 2015; **10**:e0128946.
77. Vaegter HB, Palsson TS, Graven-Nielsen T. Facilitated pronociceptive pain mechanisms in radiating back pain compared with localized back pain. *J Pain* 2017; **18**:973-83.
78. Coggon D, Ntani G, Palmer KT, *et al.* Patterns of multisite pain and associations with risk factors. *Pain* 2013; **154**:1769-77.

79. Gerhardt A, Eich W, Treede RD, Tesarz J. Conditioned pain modulation in patients with nonspecific chronic back pain with chronic local pain, chronic widespread pain, and fibromyalgia. *Pain* 2017; **158**:430-39.
80. Alappattu MJ, George SZ, Robinson ME, *et al.* Painful intercourse is significantly associated with evoked pain perception and cognitive aspects of pain in women with pelvic pain. *Sex Med* 2015; **3**:14-23.
81. Gil-Martínez A, Grande-Alonso M, La Touche R, *et al.* Psychosocial and somatosensory factors in women with chronic migraine and painful temporomandibular disorders. *Pain Res Manag* 2016; **2016**:3945673.
82. Lemming D, Graven-Nielsen T, Sörensen J, *et al.* Widespread pain hypersensitivity and facilitated temporal summation of deep tissue pain in whiplash associated disorder: an explorative study of women. *J Rehabil Med* 2012; **44**:648-57.
83. Chua N, Timmerman H, Vissers K, OH W-S. Multi-modal quantitative sensory testing in patients with unilateral chronic neck pain: An exploratory study. *Journal of Musculoskeletal Pain* 2012; **20**:292-99.
84. Robinson ME, Wise EA, Gagnon C, *et al.* Influences of gender role and anxiety on sex differences in temporal summation of pain. *J Pain* 2004; **5**:77-82.
85. Rolke R, Magerl W, Campbell KA, *et al.* Quantitative sensory testing: a comprehensive protocol for clinical trials. *Eur J Pain* 2006; **10**:77-88.
86. Nahman-Averbuch H, Yarnitsky D, Sprecher E, *et al.* Relationship between personality traits and endogenous analgesia: the role of harm avoidance. *Pain Pract* 2016; **16**:38-45.
87. Goubert D, Danneels L, Cagnie B, *et al.* Effect of pain induction or pain reduction on conditioned pain modulation in adults: A systematic Review. *Pain Pract* 2015; **15**:765-77.

88. Kuppens K, Hans G, Roussel N, *et al.* Sensory processing and central pain modulation in patients with chronic shoulder pain: A case-control study. *Scand J Med Sci Sports* 2018; **28**:1183-1192
89. Hendy AM, Lamon S. The Cross-Education Phenomenon: Brain and Beyond. *Front Physiol* 2017; **8**:297.
90. Howatson G, van Someren KA. Evidence of a contralateral repeated bout effect after maximal eccentric contractions. *Eur J Appl Physiol* 2007; **101**:207-14.
91. Andersen LL, Saervoll CA, Mortensen OS, *et al.* Effectiveness of small daily amounts of progressive resistance training for frequent neck/shoulder pain: randomised controlled trial. *Pain* 2011; **152**:440-6.
92. Koltyn KF, Knauf MT, Brellenthin AG. Temporal summation of heat pain modulated by isometric exercise. *Eur J Pain* 2013; **17**:1005-11.
93. Vaegter HB, Handberg G, Graven-Nielsen T. Isometric exercises reduce temporal summation of pressure pain in humans. *Eur J Pain* 2015; **19**:973-83.
94. Bishop MD, George SZ, Robinson ME. Dynamic, but not static, pain sensitivity predicts exercise-induced muscle pain: covariation of temporal sensory summation and pain intensity. *Neurosci Lett* 2012; **526**:1-4.
95. Torisu T, Wang K, Svensson P, *et al.* Effects of eccentric jaw exercise on temporal summation in jaw-closing muscles of healthy subjects. *Eur J Pain* 2010; **14**:719-24.
96. Ickmans K, Malfliet A, De Kooning M, *et al.* Lack of gender and age differences in pain measurements following exercise in people with chronic whiplash-associated disorders. *Pain Physician* 2017; **20**:E829-E40.
97. Vaegter HB, Handberg G, Graven-Nielsen T. Hypoalgesia after exercise and the cold pressor test is reduced in chronic musculoskeletal pain patients with high pain sensitivity. *Clin J Pain* 2016; **32**:58-69.

98. Brellenthin AG, Crombie KM, Cook DB, *et al.* Psychosocial Influences on Exercise-Induced Hypoalgesia. *Pain Med* 2017; **18**:538-50.
99. Vaegter HB, Handberg G, Graven-Nielsen T. Similarities between exercise-induced hypoalgesia and conditioned pain modulation in humans. *Pain* 2014; **155**:158-67.
100. Ray CA, Carter JR. Central modulation of exercise-induced muscle pain in humans. *J Physiol* 2007; **585**:287-94.
101. Karlsson L, Gerdle B, Ghafouri B, *et al.* Intramuscular pain modulatory substances before and after exercise in women with chronic neck pain. *Eur J Pain* 2015; **19**:1075-85.
102. Grooten WJ, Mulder M, Josephson M, A *et al.* The influence of work-related exposures on the prognosis of neck/shoulder pain. *Eur Spine J* 2007; **16**:2083-91.
103. Naugle KM, Riley JL. Self-reported physical activity predicts pain inhibitory and facilitatory function. *Med Sci Sports Exerc* 2014; **46**:622-9.

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FIGURE LEGENDS

Figure 1 Flowchart diagram of participants

Figure 2 Mean Pressure Pain Threshold (PPT)

2A Baseline PPT in controls (white) and neck/shoulder pain group (black).

2B PPT in females with neck/shoulder pain before (grey) and after intervention (black).

UT (upper trapezius), ECRB (extensor carpi radialis brevis) and ECU (extensor carpi ulnaris)

Figure 3 Mean cuff pain detection threshold (PDT) and pain tolerance threshold (PTT)

3A Baseline PDT and PTT in controls (white), and neck/shoulder pain group (black).

3B PDT and PPT in females with neck/shoulder pain before (grey) and after intervention (black).

Figure 4 Temporal summation of pain, as the difference in the mean of the visual analogue scale (VAS) scores during 10 repeated cuff stimulations between VAS-II (stimulations 8 to 10) and VAS-I (stimulations 1 to 4).

4A Baseline values in controls (white), and females with neck/shoulder pain (black).

4B Temporal summation of pain in females with neck/shoulder pain before (grey) and after intervention (black)

Figure 5 Conditioned pain modulation, expressed as differences in pain detection thresholds (PDTs) and PDT percentage increase from before vs during conditioning stimulation.

Control group is represented in white, and neck/shoulder pain group is represented in grey (baseline) and black (after intervention).

TABLES

Table 1. Baseline clinical and demographic outcome measures

	Neck / Shoulder Pain Group (n=20)	Control Group (n=20)	<i>P</i> Values
Age (years)	46.8 ± 1.3	41.7 ± 2.5	0.076
Height (cm)	169.15 ± 1.34	169.15 ± 1.61	1.00
Weight (kg)	70.07 ± 3.12	64.35 ± 2.09	0.137
Body Mass Index (kg/cm ²)	24.42 ± 0.96	22.42 ± 0.56	0.134
Hand dominance:right; left; ambidextrous;% (n)	90%(18); 5%(1); 5%(1)	75%(15); 20%(4); 5%(1)	0.420
Working hours per week	35.2 ± 1.2	34.6 ± 1.5	0.742
Years working with computers	22.87 ± 2.99	14.60 ± 2.13	0.030
Pain duration (months) [†]	120 (39-207)	N/A	-----
Most painful side: right; left; %(n)	70% (14); 30% (6)	N/A	-----
Nordic MSKQ (neck)	16.9 ± 0.7	10.1 ± 1.07	< 0.001
Nordic MSK (shoulder)	16.3 ± 1.43	8.7 ± 1.39	< 0.001
NPRS (worst pain last 24 hours)	5.30 ± 0.47	0.27 ± 0.12	< 0.001
NPRS (pain average last week)	5.30 ± 0.42	0.75 ± 0.19	< 0.001
Neck Disability Index (0-50)	10.95 ± 1.51	1.15 ± 0.31	< 0.001
DASH	15.44 ± 2.16	2.24 ± 0.95	< 0.001

DASH (work module)	13.43 ± 3.93	0.93 ± 0.68	0.001
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Data are expressed as mean ± standard error of the mean, or in percentage frequencies (%)

[†] Median and interquartile range. MSKQ, Musculoskeletal Questionnaire; NPRS, Numeric Pain Rating Scale; DASH, The Disabilities of the Arm, Shoulder and Hand Questionnaire

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Table 2. Within-group differences in self-reported neck/shoulder pain and disability

Neck / Shoulder Pain	Before	After	3-month	6-month	P
Group (n=19)	Intervention	Intervention	follow-up	follow-up	value
NPRS (worst pain last 24 hours)	5.3 ± 0.5 (4.2 - 6.3)	1.9 ± 0.4 (1 - 2.8)	2.3 ± 0.4 (1.5 - 3.2)	2.2 ± 0.6 (0.9 - 3.5)	0.002
NPRS (pain average last week)	5.3 ± 0.4 (4.4 - 6.3)	2.2 ± 0.4 (1.6 - 2.9)	2.9 ± 0.4 (2 - 3.8)	2.8 ± 0.4 (1.9 - 3.7)	0.002
Neck Disability Index (0-50)	10.9 ± 1.5 (7.5 - 14.1)	6.4 ± 0.6 (5.1 - 7.8)	-----	-----	0.014
DASH	15.7 ± 2.3 (11 - 20.5)	9.8 ± 1.7 (6.3 - 13.4)	-----	-----	0.002
DASH (work module)	13.8 ± 4.1 (5.1 - 22.5)	7.9 ± 2.9 (1.8 - 14)	-----	-----	0.107

NPRS, Numeric Pain Rating Scale; DASH, The Disabilities of the Arm, Shoulder and Hand Questionnaire

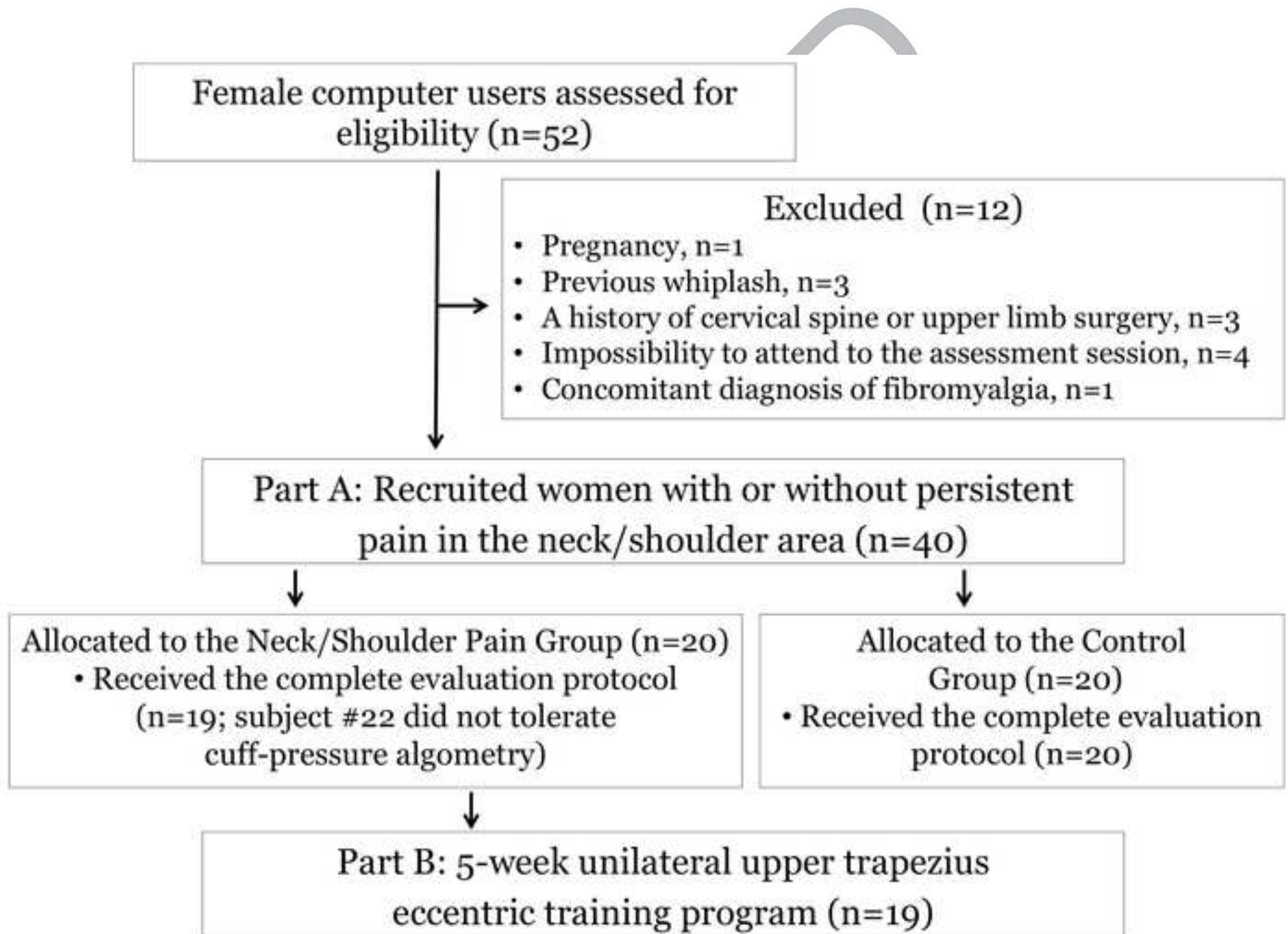
Table 3. Correlation coefficients between clinical data (years with computer, working hours per week, and pain duration), clinical outcomes (pain intensities, and neck-shoulder disability), pressure pain sensitivity over the painful side (PPT UT), and central pain measures (TSP and CPM) in females with neck/shoulder pain

	Years with computer s	Workin g hours per week	Pain duratio n	NPRS (last 24 h)	NPR S (last week)	DAS H	NDI	PPT UT	TSP	CP M
Years with computer s	1	–	–	–	–	–	–	–	–	–
Working hours per week	0.191	1	–	–	–	–	–	–	–	–
Pain duration	0.643	0.414	1	–	–	–	–	–	–	–
NPRS (last 24 h)	0.176	-0.339	-0.089	1	–	–	–	–	–	–
NPRS (last week)	0.147	-0.358	-0.333	0.731 *	1	–	–	–	–	–
DASH	0.148	0.062	-0.259	0.260	0.294	1	–	–	–	–

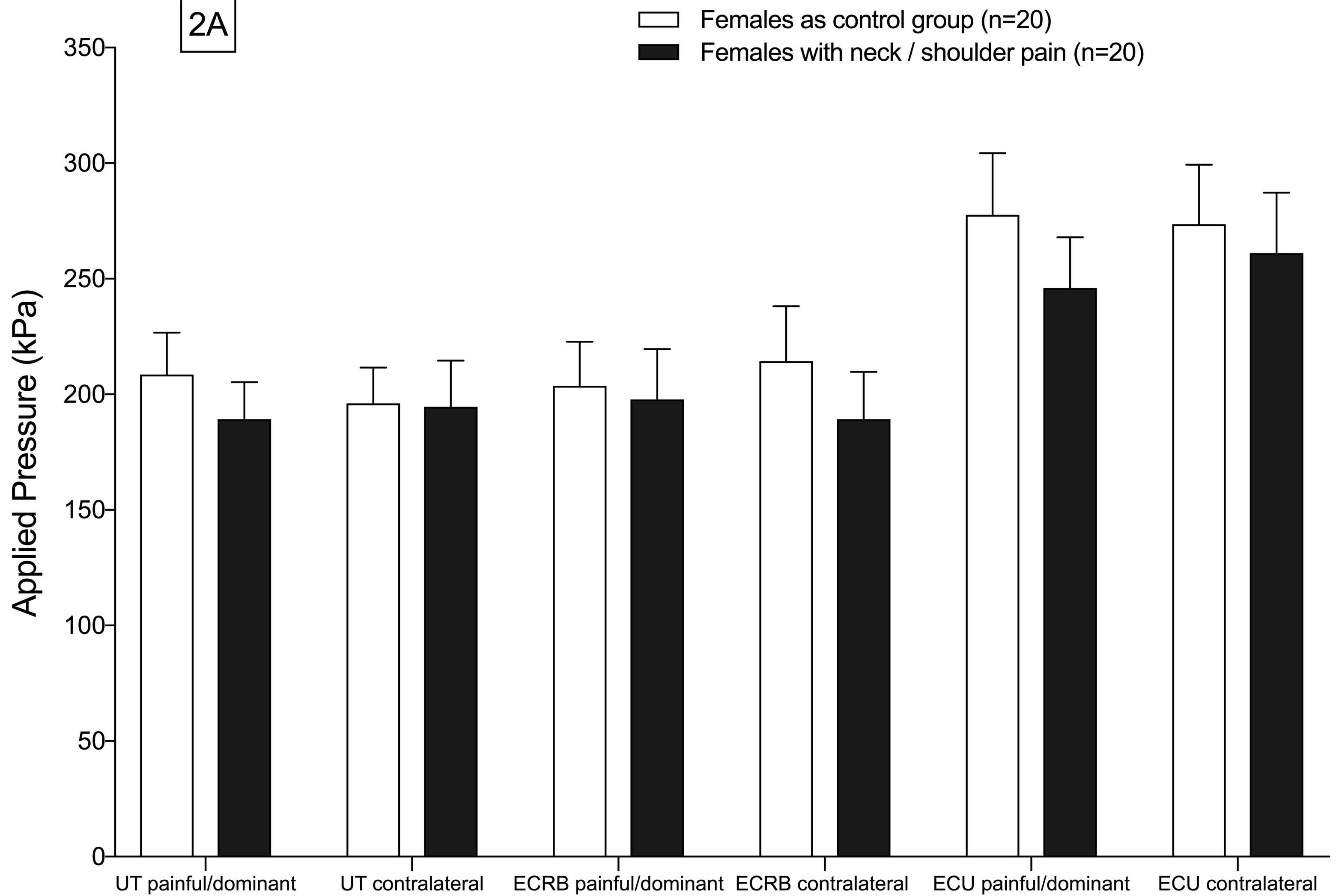
NDI	-0.091	0.252	-0.135	0.205	0.209	0.074	1	–	–	–
PPT UT	-0.270	0.041	0.250	-0.090	-	0.242	0.24	1	–	–
				0.295			6			
			-0.210	0.199	0.245	0.107	-	-	1	–
TSP	-0.297	-0.246					0.32	0.35		
							1	7		
			0.430	-0.403	-	-	-	-	-	1
CPM	.091	0.253			0.460	0.627	0.16	0.14	0.07	
					*		9	5	8	

* p < 0.001 significant correlation after Bonferroni correction

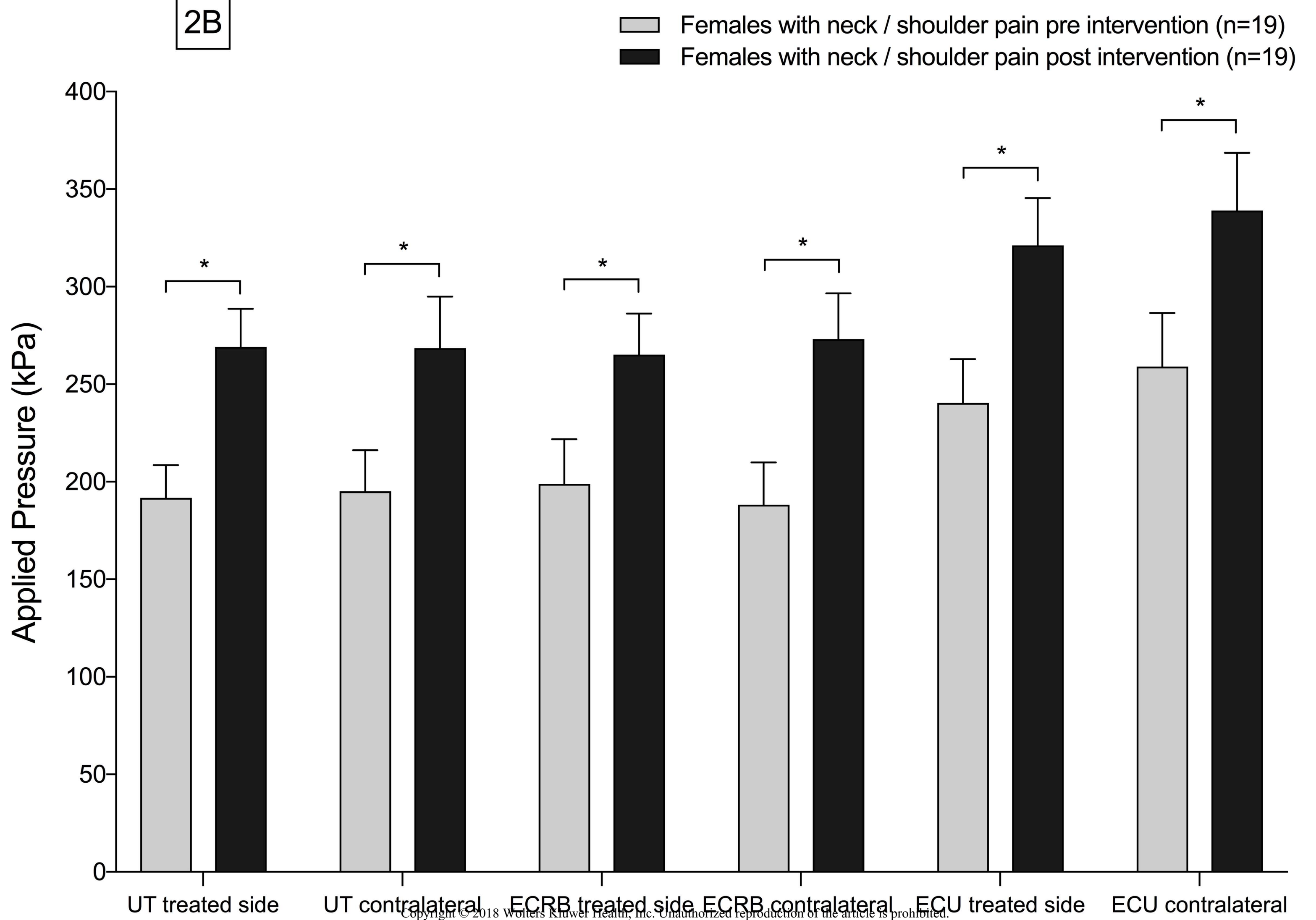
NPRS, Numeric Pain Rating Scale; DASH, The Disabilities of the Arm, Shoulder and Hand Questionnaire; NDI, The Neck Disability Index; PPT, Pressure Pain Threshold; UT, Upper Trapezius; TSP, Temporal Summation of Pain; CPM, Conditioned Pain Modulation



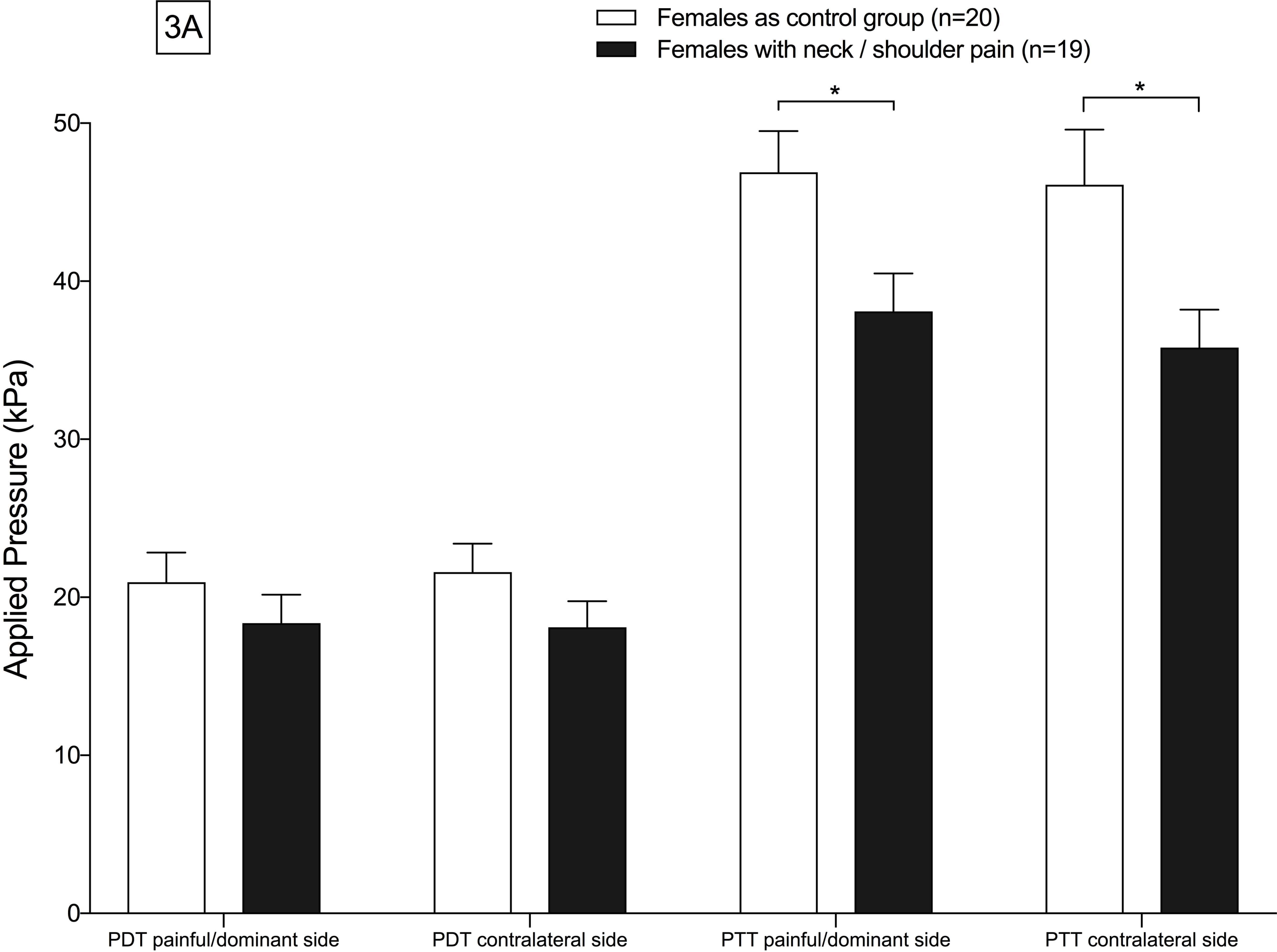
2A



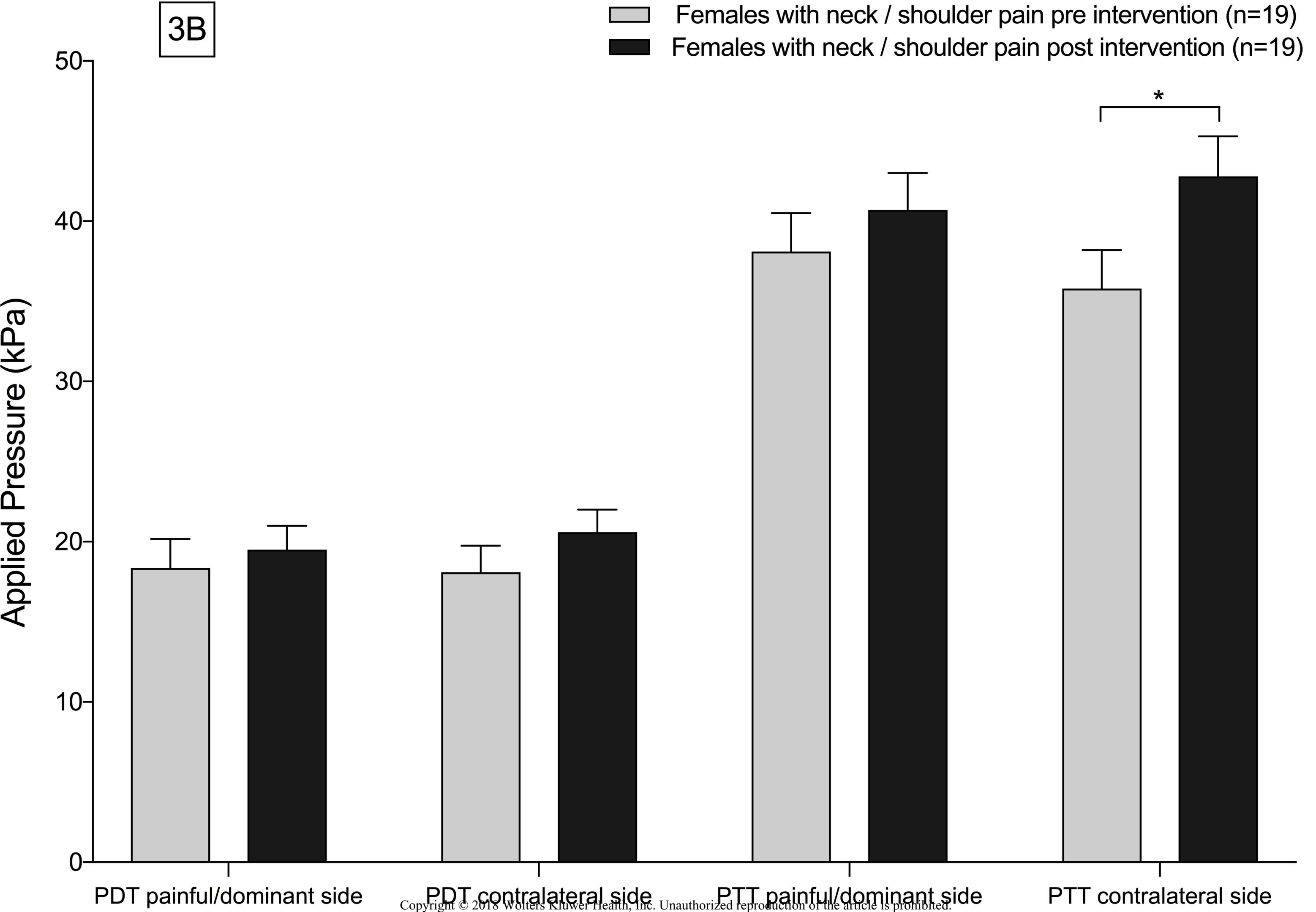
2B

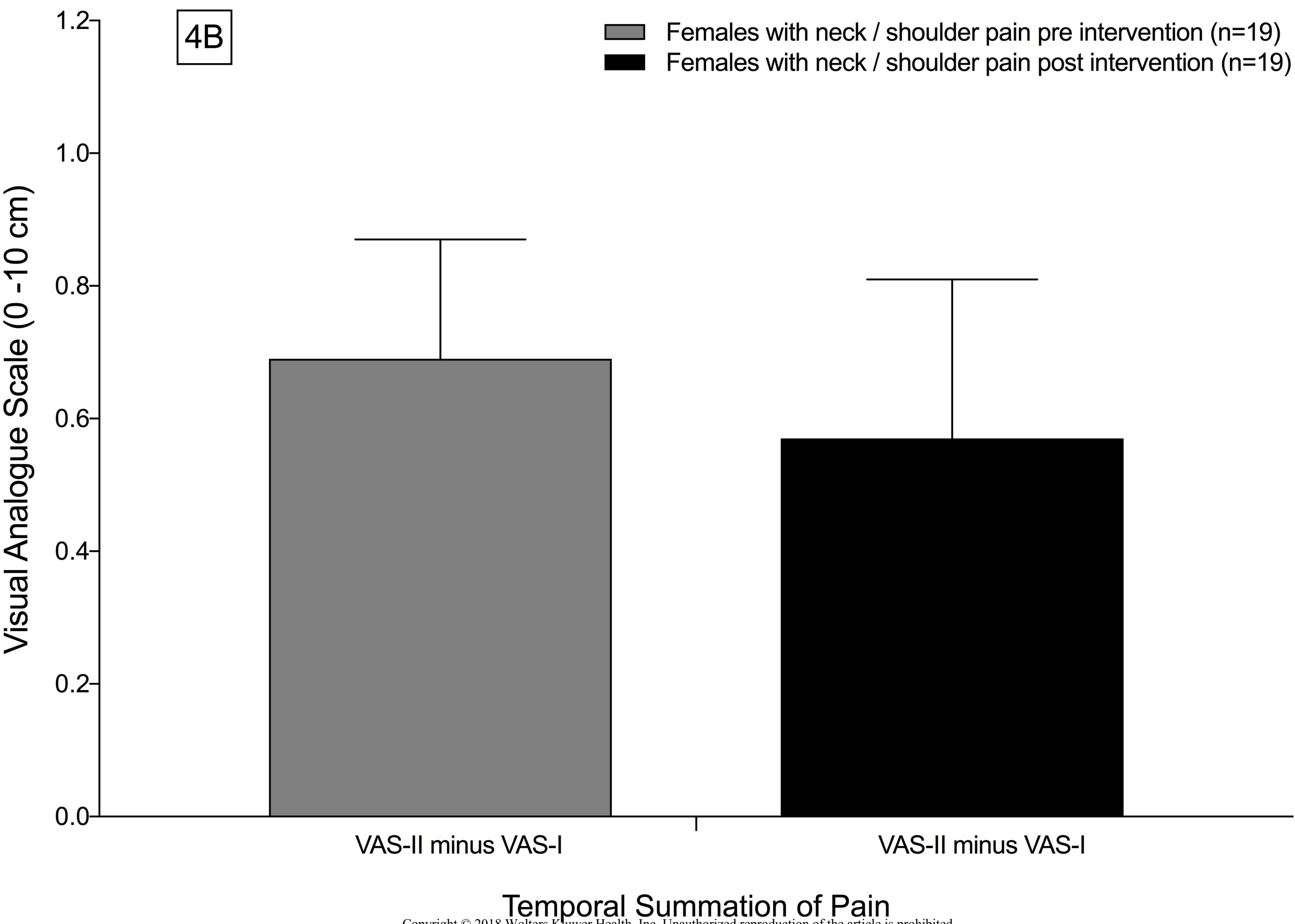
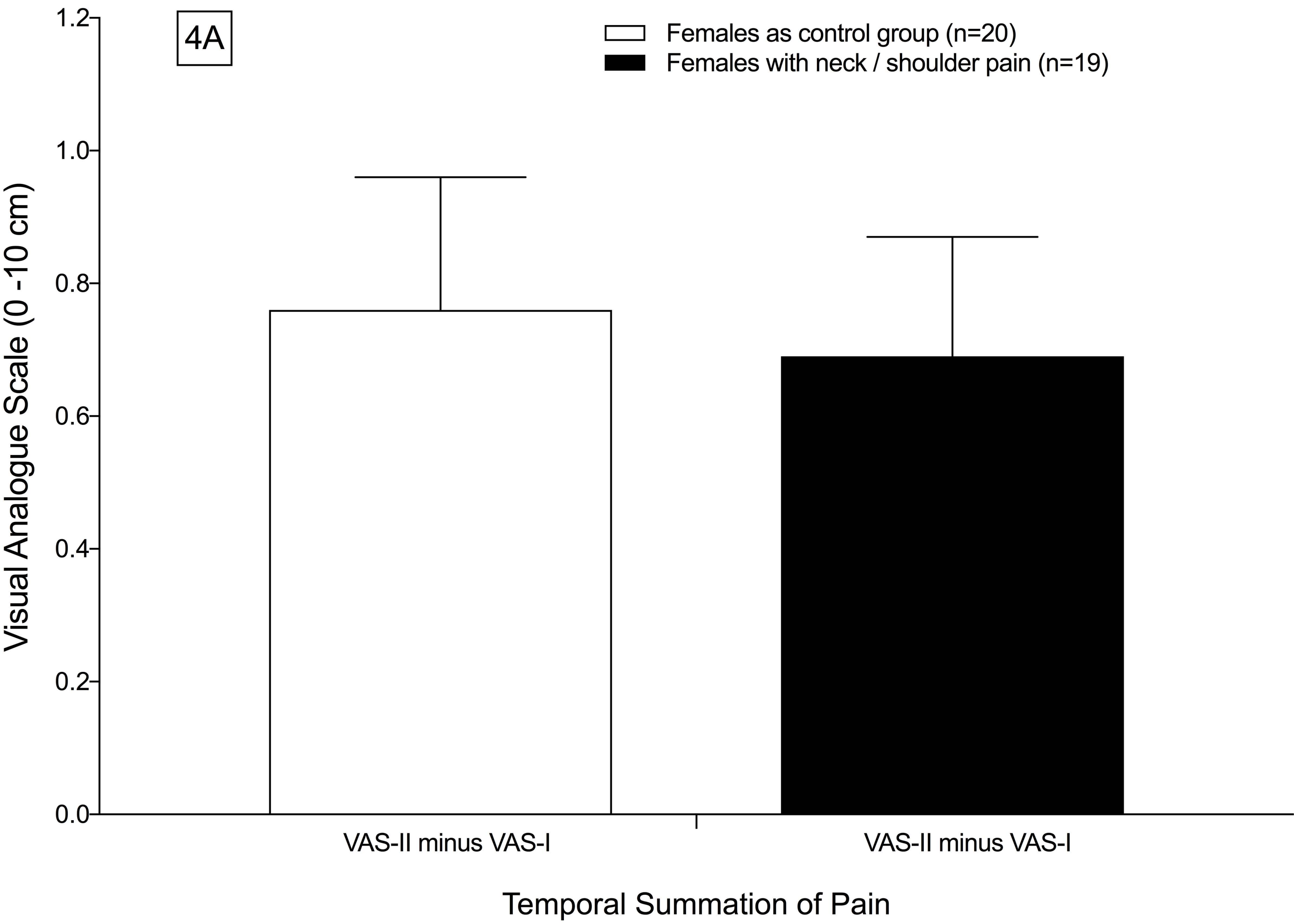


3A

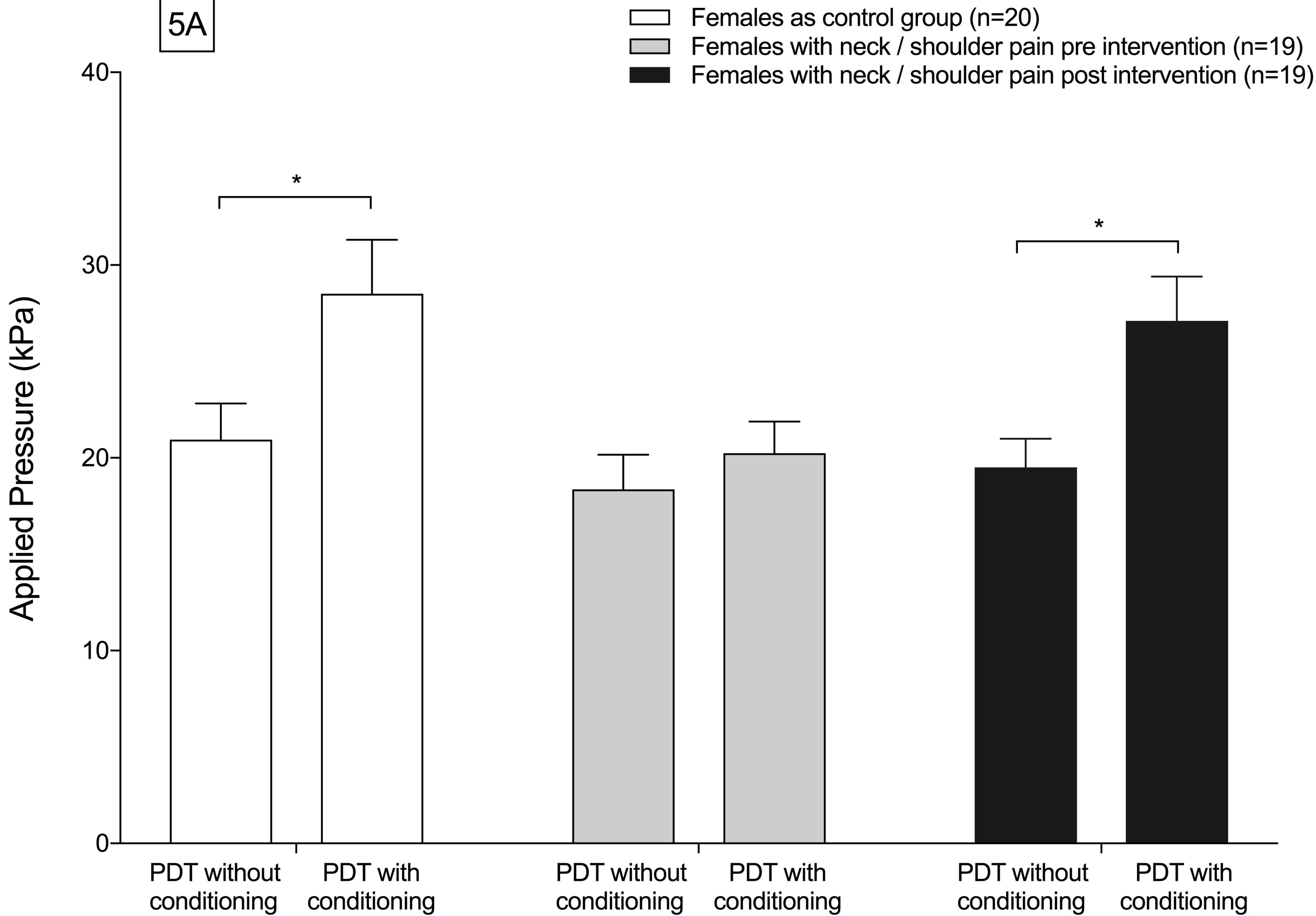


3B





5A



5B

